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<p>(21) International Application Number: PCT/EP90/01537 (22) International Filing Date: 12 September 1990 (12.09.90) (30) Priority data: P 39 30 770.0 14 September 1989 (14.09.89) DE (71)(72) Applicant and Inventor: SCHÖNER, Wolfgang [DE/ DE]; Grundmühle 1, D-3510 Hannoversch-Münden (DE). (74) Agents: STERNAGEL, Hans-Günther et al.; Sander Aue 30, D-5060 Bergisch Gladbach 2 (DE).</p>		<p>(81) Designated States: AT (European patent), BE (European patent), CA, CH (European patent), DE (European patent)*, DK (European patent), ES (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: IMPLANTABLE CATHETER MADE OF HIGH COLD FLOWN MATERIAL</p> <p>(57) Abstract</p> <p>Implantable catheter made of medically tolerated synthetic material, whose thermoplastic polymer has an excellent cold flow at 34 °C to 40 °C under a weight load of 40 g/0.2 mm², so that, in the case of a continuous tensile load for 63 days, the initial length of the catheter increases by at least 50 % in the direction of the longitudinal axis, the extruded catheter tube consisting of three layers connected to each other and arranged coaxially, and the middle layer containing a radiopaque pigment.</p>		

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IMPLANTABLE CATHETER MADE OF HIGH
COLD FLOWN MATERIAL

The invention relates to an implantable catheter made of medically tolerated synthetic material, the elastic, plastically deformable polymer having a particularly high cold flow.

DE-A-2,902,434 discloses a method for the deformation of vessel implants and for the preparation of tissue incorporation, in particular of umbilical cords. For the purpose of deformation, the umbilical cord is first dehydrated and then treated with an aldehyde. In order to facilitate the incorporation of the implant, the surface is roughened mechanically.

DE-A-3,239,318 deals with a formable polyurethane elastomer which has good blood tolerability and which is the product of reaction of an aliphatic organic diisocyanate, a polyether polyol of high molecular weight and 1,4-butanediol as chain lengthener. By using two equivalents of diisocyanate per equivalent of the polyol of high molecular weight, an elastomeric material with a Shore A hardness of 70 is obtained. The polyurethane can be used for catheters.

In the DSG Report No. 17 of January 1984 (The Donalds Gilmore Laboratories) on Pellethane 2363, polyether/polyurethane resins which comply with the FDA

requirements are described for medical purposes. The starting materials used are polytetramethylene ether glycol, 1,4-butanediol and diphenylmethane diisocyanate. The polyurethane can be made radiopaque by adding pigments such as BaSO₄. Despite the biological tolerability, express reference is made to the fact that, on account of the lack of long-term data, use for implants is not recommended.

The purpose of the known biologically tolerated substances was to produce continuously elastic, thermoplastic polymers which are dimensionally stable.

One disadvantage of known implantable catheters made of medically tolerated synthetic materials consists in the fact that their length in the implanted state is virtually constant. There are cases, however, when changes in the size of the body of the patient, for example growth, results in a failure of the implanted tube system or of the catheter, because the catheter does not grow too and the implanted lumen connection necessary for maintaining the body functions is broken. Thus, it is necessary, for example in the case of neonates or infants with disorders of the cerebrospinal fluid circulation in the cranial region, to drain excess fluid from the ventricle chamber system by means of a catheter, for example into the peritoneal cavity. Since disorders of this type cannot at present be rectified other than by implanting a catheter, the growth of the body with increasing age has the result that an implanted catheter becomes too short and the drainage or feeding of fluid from or, respectively, to certain areas of the body is impaired or interrupted. Since replacement of catheters which may be too short cannot in most cases be carried out in good time, the failure of the artificial lumen connections inside the body often has serious consequences on the patient's health.

The aim of the invention is to produce a catheter whose

length in the implanted state increases in line with the growth of the body, so that a permanent functioning of the lumen connection produced in the body by means of the catheter is ensured.

This aim is achieved by means of an implantable catheter made of medically tolerated, elastic, plastically deformable synthetic material, characterized in that the extruded catheter tube consists of three layers, connected to each other and arranged coaxially, of one polymer or a mixture of polymers, whose cold flow at 34°C to 40°C under a weight load of 40 g/0.2 mm² for 63 days results in an increase in the initial length of at least 50% in the direction of the longitudinal axis, the middle layer contains a radiopaque pigment, and the smooth outer surface of the catheter tube is slightly roughened at one end and at a distance from the other end over a length of approximately 5 mm.

The so-called cold flow is understood as the flow of a polymer material under pressure or tensile load at temperatures below the glass transition temperature of the polymer. Cold flow is regarded by specialists as a frequently undesired property of polymer materials, which property, however, can be diminished, but not completely suppressed, in the case of relatively soft polymers by appropriate selection of the monomers, certain polymerization conditions and, where appropriate, crosslinking. Cold flow is a measurement of the plastic, irreversible deformability of the polymer in the region of room temperature. The Shore hardness and modulus of elasticity are measurements of the elastic behaviour of polymers, but they do not permit any conclusions to be made as regards the irreversible plastic deformability below the glass transition temperature.

It has been found, very surprisingly, that cold flow - this property of polymers which has hitherto been regarded by most specialists as a disadvantage - can be used

to achieve the aim according to the invention if, for implantable catheters, a medically tolerated elastic, plastically deformable polymer is chosen which has an excellent cold flow. The so-called cold flow should, in the case of a permanent weight load (tensile load) on the catheter tube in the longitudinal direction of $40 \text{ g}/0.2 \text{ mm}^2$ cross-sectional surface of the polymer material, increase the initial length by at least 50% in 63 days, without thereby causing any damage to the catheter tube. In order to permit the incorporation of the catheter according to the invention at the desired sites, it has proven expedient to slightly roughen the outer surface of the catheter tube, which is produced smooth by means of extrusion, in order to promote the attachment of fibroblasts following implantation. This leads to an incorporation of the catheter in the tissue, so that the catheter is fixed at the incorporated sites. If, as a result of a change in the size of the patient's body, the distance between the fixation points of the catheter tube now changes, the latter becomes subject to tensile stress. As a result of the excellent cold flow of the polymer, the tensile stress decreases again as the catheter lengthens. The cold flow permits an appropriate increase in the length of the implanted catheter tube between the fixation points inside the body.

Suitable for the catheter according to the invention are relatively soft, plastically deformable polymers, which should be neither hydrolysable nor degradable fermentatively/enzymatically. Suitable medically tolerated polymers are thermoplastics, such as aliphatic polyetherurethanes, polyamides, low-density polyethylene (LDPE), polypropylene and mixtures thereof.

The polymers may be both homopolymers as well as copolymers which are sufficiently resistant to hydrolysis. Aliphatic polyetherurethanes from polyalkylene glycol ethers and suitable organic aliphatic diisocyanates, such as diphenylmethane-4,4-diisocyanate, which may optionally

be loosely crosslinked with 1,4-butanediol, are preferred. In order to obtain a sufficiently soft, plastically deformable polyurethane, it is necessary, for the reaction between the diol and the polyisocyanate, to use more than two equivalents of polyisocyanate per equivalent of diol. A polyisocyanate:diol equivalence ratio of >2 to 6 is preferred.

A very particularly preferred polyalkylene glycol is polytetramethylene ether glycol of the formula $\text{HO}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O})_n\text{H}$, in which n is an integer of 2 or more. However, other polyether alcohols can also be used for the reaction with diisocyanates to produce loosely crosslinked polyurethanes with the excellent cold flow. The reaction of 1,4-butanediol and other diols with suitable aliphatic diisocyanates to give linear, elastic polyurethanes with good hydrolysis resistance and the desired plastic deformability and the necessary cold flow poses no problems to the person skilled in the art. As regards the polyamides, those types with low crystallization are particularly suitable for the catheters according to the invention.

In order to facilitate the implantation and the correct positioning of the catheters according to the invention, the polymer is provided with a radiopaque material before extrusion of the catheter tube. Suitable radiopaque materials are, for example, BaSO_4 , bismuth compounds, tungsten or tungsten compounds, tantalum powder or noble metals in very fine distribution. The pigment portion can amount to between 1% by weight and 20% by weight relative to the total weight of the polymer provided with filler. In order to facilitate the extrusion and to stabilize this long-term, auxiliaries such as stabilizers and other medically tolerated auxiliaries can be added to the polymers during processing.

In order to prevent interactions between the radiopaque material and the tissue following implantation, the

polymer made radiopaque is provided on the outside and the inside of the catheter tube with a protective layer of the same, or a compatible, plastically deformable polymer without radiopaque pigment. The coaxial arrangement of the protective layers can be produced in a particularly simple way by coextrusion through appropriate tubular dies. It is preferable to design the outer layers or protective layers thinner than the middle layer containing pigment. The multilayer design of the catheter tube has the additional advantage that the risk of breaking is reduced. The residual elasticity of the polymer, which remains in spite of the plastic deformability of the polymer, makes it possible to bend the catheter tube freely 360° with a bending diameter of 5 mm without breaking.

The catheter can be designed both as a single-lumen catheter and with several lumina. In the case of a single-lumen catheter, it is preferable to have an internal diameter of the catheter tube of 0.8 mm to 1.8 mm and a wall thickness of 0.1 mm to 0.5 mm, preferably to 0.3 mm.

The invention also includes a method for producing a catheter made of medically tolerated synthetic material by means of coextrusion, at temperatures of 150°C to 170°C, of the polymer mixture through an appropriate die made of Teflon-coated metal, an alloy available under the name Hostalloy for producing extrusion dies. In order to obtain an especially smooth outer surface of the catheter tube, which prevents undesired firm attachment of fibroblasts, it is preferable to cool the extrudate with cold water flowing in the laminar direction. After drying of the extruded tube, this can be divided up into catheters of the desired length, and roughening can be carried out on the desired areas of the outer surface. The surface is preferably slightly roughened over a length of about 5 mm by means of slightly damaging the smooth surface skin formed on extrusion.

It is also possible, on extrusion, not to completely degas the polymer for the outer layer, or else to charge it with an inert gas, in order to bring about bubble formation in the outer layer. These bubbles burst during bending of the catheter and afford a roughened surface. If imperfections of this type are produced at intervals of about 40 cm on extrusion, then catheter lengths can be cut which exhibit roughening at the desired areas. In order to permit fixation of the catheter according to the invention following implantation, the catheter is roughened at one end and is roughened either at the opposite end or, preferably, at a certain distance from the other end.

The catheters according to the invention can be used for producing artificial lumen connections inside the body.

The catheter according to the invention is particularly suitable for the treatment of internal as well as external communicating and obstructive hydrocephalus of every genesis (following intracranial haemorrhaging, following infections, in tumour diseases, intracranial space requirements, cerebrovascular disorders, stenosis of the aqueduct of the cerebrum, and in malformations) in children and adults. Furthermore the catheter can be used for the treatment of chronic intracranial as well as intraspinal and intramedullary accumulations of fluid by means of drainage into the peritoneal cavity or into the venous system or into the right heart or the right atrium of the heart.

Example

Establishment of a ventriculo-peritoneal shunt using a pressure- or flow-controlled valve.

A cut is made in the skin to the right or left alongside the median line (about 2 cm) directly over the coronal suture of the cranium. Immediately in front of the coronal suture, a bore 0.5 to 1.5 cm in size is made in the cranial vault and the dura mater is exposed. Follow-

ing punctiform coagulation and perforation of the dura mater, a catheter with a blind end and with no sharp edges, 3.5 to 7 cm in length, with 2 to 20 lateral holes of any size, and made of the same material as the "peritoneal-atrial catheter" is advanced via the opening in the dura mater through the frontal brain into the right or left lateral ventricle, and the brain-remote end is firmly connected to the valve provided (manufacturer PS-Medical). After making a skin incision above the umbilicus over one of the two straight muscles of the abdomen, the outer muscle fascia is incised and a trocar is inserted, by means of which the peritoneal cavity is finally punctured by perforation of the visceral muscle fascia and of the peritoneum. The hollow-needle-type trocar with a cross-section of at least 3 mm is used for advancing one end of a catheter according to the invention, which is up to 90 cm in length and is made of elastic polymers (silicone elastomer from Dow Corning), into the peritoneal cavity by a maximum length of 20 cm. A lance-shaped instrument is then used to form a channel in the subcutaneous fatty tissue via a retroauricular auxiliary incision as far as the free valve support, and a suture is threaded in in such a way that a subcutaneous attachment of the catheter partially lowered into the peritoneal cavity is possible. The free head-side catheter end is connected in a non-detachable manner to the free valve support. After checking the functioning, the skin wounds are sewn up sterilized.

PATENT CLAIMS

1. Implantable catheter made of medically tolerated, elastic, plastically deformable synthetic material, characterized in that the extruded catheter tube consists of three layers, connected to each other and arranged coaxially, of one polymer or a mixture of polymers, whose cold flow at 34°C to 40°C under a weight load of 40 g/0.2 mm² for 63 days results in an increase in the initial length of at least 50% in the direction of the longitudinal axis, the middle layer contains a radiopaque pigment, and the smooth outer surface of the catheter tube is slightly roughened at one end and at a distance from the other end, in each case over a length of about 5 mm.
2. Catheter according to Claim 1, characterized in that the outer layers of the catheter tube are designed thinner than the middle layer containing pigment.
3. Catheter according to Claim 1 or 2, characterized in that the polymer is aliphatic polyurethane, polyamide, low-density polyethylene (LDPE), polypropylene or a mixture of these polymers.
4. Catheter according to Claim 3, characterized in that the elastic, aliphatic polyetherurethane was formed from polyalkylene glycol ethers, where appropriate 1,4-butane-diol and diphenylmethane-4,4-diisocyanate.
5. Catheter according to each of claims 1 to 4, characterized in that the catheter has one lumen with an internal diameter of the catheter tube of 0.8 mm to 1.8 mm, and the wall thickness is 0.1 mm to 0.5 mm.
6. Catheter according to each of Claims 1 to 5, characterized in that the catheter tube has several parallel lumina.
7. Method for producing a catheter according to each of

Claims 1 to 7, by coextrusion of the polymers through a multilayer tubular die, which optionally has additional openings for the formation of several lumina, made of Teflon-coated metal, Hastalloy, at temperatures of 150°C to 170°C, with cooling of the extrudate in cold water flowing in the laminar direction, drying of the extrudate tube, dividing into catheters of the desired length, and roughening of the outer surface over a length of 5 mm at one end and at a distance from the other end by damaging the smooth surface skin formed on extrusion.

8. Use of the implantable catheter according to Claims 1 to 6, for producing artificial lumen connections inside the body.

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INTERNATIONAL SEARCH REPORT

International Application No. PCT/EP 90/01537

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC⁵: A 61 M 25/00, A 61 L 29/00

II. FIELDS SEARCHED

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A 61 M, A 61 F, A 61 L

Documentation Searched other than Minimum Documentation
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III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹

Category ⁹ | Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹² | Relevant to Claim No. ¹³

A US, A, 4627844 (SCHMITT)
9 December 1986

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A US, A, 4282876 (FLYNN)
11 August 1981

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A US, A, 4211741 (OSTOICH)
8 July 1980

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A US, A, 3623484 (SCHULTE)
30 November 1971

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IV. CERTIFICATION

Date of the Actual Completion of the International Search

10th January 1991

Date of Mailing of this International Search Report

25 JAN 1991

International Searching Authority

EUROPEAN PATENT OFFICE

Signature of Authorized Officer

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

EP 9001537
SA 40235

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4627844	09-12-86	None	
US-A- 4282876	11-08-81	US-A- 4250072	10-02-81
		US-A- 4283447	11-08-81
US-A- 4211741	08-07-80	None	
US-A- 3623484	30-11-71	US-A- 3738365	12-06-73

EP 9001537

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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